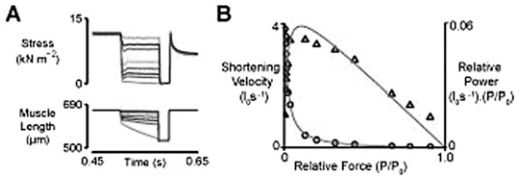
values ranging from 9.0 to 4.5. The rates of tension recovery (k_{tr}) measured in pCa 4.5 solution were significantly higher ($p<0.002$, 2-way ANOVA) in the preparations isolated from the HLU animals than in preparations isolated from the control groups (k_{tr} mean values ± SEM measured in pCa 4.5 were: 7.45 ± 0.37 s^{-1} for female control; 9.54 ± 0.50 s^{-1} female HLU; 7.70 ± 0.46 s^{-1} male control and 8.42 ± 0.37 s^{-1} male HLU). The relative content of slower beta-Myosin Heavy Chain decreased in both HLU groups compared to the corresponding control groups ($p<0.01$, 2-way ANOVA). There was no interaction for this parameter between sex and unloading condition ($p=0.93$, 2-way ANOVA). The heart-to-body weight ratios increased significantly in the HLU groups ($p<0.0001$, 2-way ANOVA) but again there was no interaction with sex ($p=0.84$, 2-way ANOVA). If similar mechanisms operate in humans, female astronauts may be more likely to develop presyncope after space-flights than male astronauts because their hearts contain a greater relative content of the alpha-Myosin Heavy Chain when they return to Earth.

1608-Pos Board B518
Molecular Mechanisms Involved in the Rescue of Severe Pulmonary Hypertension by Genistein Therapy
Humann Matori, Soban Umar, Rod Partow-Navid, Andrea Iorga, Rangarajan Nadadur, Reza Foroughi, Michelle Afkhami, Mansoureh Eghbali.
Previously, we showed that genistein, a soy isoflavone, rescued severe pulmonary hypertension(PH). However, the mechanisms involved in the rescue were largely unknown. Here, we investigated possible mechanisms of genistein rescue of PH. We induced PH in rats using a single subcutaneous injection of monocrotaline(MCT, 60 mg/kg). By day 21, rats developed severe PH. At this time point, we started genistein therapy(1 mg/kg/day, subcutaneous) to one group(GEN) until day 30. The other group was left untreated and developed RV failure by day 30(MCT group). The control group(CTRL) received saline. At day 30, cardiac catheterization was performed to assess right ventricular pressure(RVP), animals were sacrificed and lungs and hearts were dissected. Immunohistochemistry, Western Blot, and RT PCR were performed. MCT group developed severe PH(RVP 31 ± 1 mmHg in CTRL, n=5 vs. 72 ± 1 mmHg in MCT, n=7). Genistein attenuated severe PH(44 ± 5 mmHg, n=8). Additionally, the RV hypertrophy index(RV/(LV+IVS)) increased(~3-fold) in MCT and was restored in GEN. We investigated the role of estrogen receptors α and β(ERα and ERβ) in genistein rescue. ERβ protein levels were significantly downregulated in lungs and RV of MCT(~2-fold and ~5-fold). Genistein restored lung and RV ERβ protein levels. ERα protein levels did not change in PH. PH led to significantly decreased capillary density in RV and VEGF protein(~2.5-fold) in both RV and lung. Genistein restored RV capillary density and significantly improved VEGF levels in RV and lung. Furthermore, we found a significant increase in lung Caspase-3(~3-fold) and pSTAT3/STAT3(~3.5-fold) proteins in MCT, which were reversed by Genistein. PH was also associated with significantly reduced lung Caveolin-1(~6-fold) protein levels that were restored in GEN. In conclusion, genistein rescues severe PH through ERβ mediated protection, preserves cardiopulmonary angiogenesis, and restores Caspase-3, pSTAT3/STAT3 and Caveolin-1 in the lungs.

1609-Pos Board B519
Light Mediated Control of Cardiac Excitability
Nobuyuki Magome.
We report the potential for photocontrol of cardiac excitation ranging from the cellular to the tissue level using the photo-sensitive compound, azobenzene trimethyammonium bromide (AzoTAB). Cells and heart tissue were collected from rats & incubated with 0.1-0.5 mM AzoTAB. Under illumination with blue light (>440 nM) and in the thermally relaxed state, the trans-isomer of AzoTAB reversibly reduced the occurrence of spontaneous activity and decreased the speed of propagating waves in cardiac myocyte monolayers, to the point of complete suppression. Illumination of near-UV light (~365 nm) changed the tertiary structure of AzoTAB to its cis-isomer form and restored monolayer excitability. In isolated atrial preparations, spontaneous activations were suppressed in the presence of AzoTAB. The activity returned after the tissue was illuminated with UV light. We conclude that AzoTAB mediated sensitization offers the potential for controlling cardiac excitation waves either uniformly or in a preferred spatial pattern. The combination of photocontrol with optical mapping techniques allows one to control and observe wave excitation patterns simultaneously without physical manipulation.

1610-Pos Board B520
Measurements of Power Output in Human Myocardium
Premi Shekar, Mihail I. Mitov, Leonardo F. Ferreira, Mark R. Bonnell, Kenneth S. Campbell.
Myocardial power output is an important determinant of ventricular function but few measurements of this parameter have been made using human tissue samples. Our group has been measuring force-velocity curves, and thus power output, in left ventricular samples obtained from patients undergoing cardiac surgery at the University of Kentucky. Multicellular preparations are prepared from previously-frozen tissue samples by mechanical homogenization and chemical permeabilization. They are then connected between a force transducer and a motor and maximally activated in a saturating [Ca2+] solution. Once force has reached steady-state, the samples are allowed to shorten against pre-set loads imposed using SLControl software. Panel A in the figure shows superposed force and muscle-length traces for an isolated myocardial preparation obtained from the heart removed from a 32 year old male during a transplant procedure. Panel B shows force-velocity and power curves calculated from these records. One of the goals of our ongoing study is to determine whether maximal power output in isolated left ventricular samples improves after patients are fitted with left ventricular assist devices. Our study will, to our knowledge, be the first to measure force-velocity and power output in preparations isolated from these patients.



1611-Pos Board B521
Myofilament Dysfunction Contributes to Impaired Myocardial Contraction in the Infarct Border Zone
Rafael Shimkunas, Guan-Ying Wang, Zhihong Zhang, Julius M. Guccione, Mark B. Ratcliffe, Anthony J. Baker.
Introduction: Following myocardial infarction, adjacent to the infarct zone, there is a border zone of hypocontractile myocardium that remains normally perfused with blood. Post-infarction cardiac remodeling may involve progressive expansion of the border zone, leading to heart failure. Despite the importance of the border zone in post-infarction pump function and heart failure progression, the cause of border zone dysfunction remains poorly understood. **Goal:** Determine the role of injury to the myofilaments in border zone dysfunction. **Methods:** We studied sheep hearts, at two and eight weeks after myocardial infarction, and unoperated controls. Myocardial contraction in-vivo was estimated with a finite element model that was optimized using myocardial strain measured by magnetic resonance imaging. In-vitro myocardial force development was measured using cardiac muscle fibers dissected from the border zone and remote zones of explanted hearts. Muscle fibers were chemically skinned and in-vitro force measured in activating solutions. **Results:** Finite element simulations suggested that border zone contractility in-vivo was reduced 50% compared to uninfarcted remote myocardium. Consistent with this, in-vitro studies found that the maximum calcium-activated force of skinned fibers from the border zone was significantly reduced (25 ± 1 mN/mm^2, n=10) compared to skinned fibers from the uninfarcted remote zone (36 ± 1 mN/mm^2, n=10, $p<0.01$). Histologically, border zone myocardium showed myocyte hypertrophy; however, there was no replacement fibrosis that could account for the reduction in myocardial force. **Conclusions:** A defect in myofilament force development contributes to impaired myocardial contraction in the infarct border zone. Injury to the myofilaments in the border zone may play a key role in heart failure progression.

1612-Pos Board B522
Effects of Cholesterol Depletion on Compartmentalized cAMP Responses in Adult Cardiac Myocytes
Shailesh R. Agarwal, David A. MacDougall, Richard Tyser, Sarah C. Calaghan, Robert D. Harvey.
The role of cholesterol-dependent lipid rafts in producing compartmentalized responses of β_1-adrenergic receptors (β_1ARs) and E-type prostaglandin receptors (EPRs) was investigated in adult rat ventricular myocytes. β_1ARs were found in lipid raft and non-lipid raft containing membrane fractions, while EPRs were only found in non-lipid raft fractions. Furthermore, β_1AR activation enhanced the L-type Ca^{2+} current ($I_{Ca\text{-}L}$), intracellular Ca^{2+} $[Ca^{2+}]_i$ transient, and myocyte shortening, while EPR activation had no effect. Cholesterol depletion by treatment with methyl-β-cyclodextrin (MβCD) did not eliminate compartmentalized behavior but significantly enhanced the sensitivity of functional responses produced by β_1ARs. In MβCD-treated cells, 1 nM isoproterenol increased $I_{Ca\text{-}L}$ by 49 +/- 8.3% (n = 5) as compared to 15 +/- 5% (n = 13) in control cells. These responses were blocked by the specific β_1AR antagonist, 100 nM CGP20712A. Similarly, β_1AR activation led to an increase in cell shortening and $[Ca^{2+}]_i$ transient from 63 +/- 13% and 18 +/- 4.1% in control cells (n = 17) to 188 +/- 19.5% and 35 +/- 4.3% in MβCD-treated cells (n = 22) respectively. Cholesterol depletion failed to elicit any effect on EPR activation. Changes in cAMP activity were also measured in intact cells using two different FRET-based biosensors: a type II PKA-based probe to monitor cAMP in